UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: February 26, 2013

SUBJECT: **Endothall:** Summary of Hazard and Science Policy Council (HASPOC) Meeting of December 19, 2012: Recommendations on the Requirement of Acute and Subchronic Neurotoxicity studies.

PC Code: 038904
Decision No.: N/A
Petition No.: N/A
Risk Assessment Type: N/A
TXR No.: 0056545
MRID No.: N/A

DP Barcode: N/A
Registration No.: N/A
Regulatory Action: N/A
Case No.: N/A
CAS No.: 145-73-3
40 CFR: §180.293

FROM: Kristin Rury, MPH
Executive Secretary, HASPOC
Health Effects Division (7509P)

THROUGH: Jess Rowland, Co-Chair
Anna Lowit, Ph.D, Co-Chair
HASPOC
Health Effects Division (7509P)

TO: John Liccione, Ph.D., Toxicologist
Seyed Tadayon, Risk Assessor
Ana Rivera-Lupiáñez, Chemist
Michael Metzger, Acting Branch Chief
Risk Assessment Branch V
Health Effects Division (7509P)

MEETING ATTENDEES

HASPOC Members: Anna Lowit, Elissa Reaves, Elizabeth Mendez, Jeff Evans, Jess Rowland, Jonathan Chen, Julie Van Alstine, Kristin Rury, PV Shah, Ray Kent

Presenters: John Liccione, Seyed Tadayon, Ana-Rivera Lupiáñez

I. PURPOSE OF MEETING

Risk Assessment Branch (RAB) V is evaluating a proposed new use of the pesticide endothall on apples. Under the current 40 CFR Part 158 data requirements, acute and subchronic neurotoxicity studies are required. The Hazard and Science Policy Council (HASPOC) met on December 19, 2012 to discuss the need for acute and subchronic neurotoxicity studies.

II. SUMMARY OF USE PROFILE & PREVIOUS RISK ASSESSMENT

Endothall is a selective contact herbicide, defoliant, desiccant, and aquatic algaecide belonging to the dicarboxylic acid chemical class. The free acid of endothall and its dipotassium and mono-N, N-dimethylalkyl-amine salts (monoalkylamine) are registered in the United States primarily as aquatic herbicides for the control of a variety of plants in water bodies, including irrigation canals with a holding period of 7 days or more. Endothall-treated water is used for irrigation purposes on non-food crops, established ornamentals, turf grass, lawns, and non-crop areas. Endothall is also registered for desiccation/de-foliation of alfalfa/clover (grown for seed only), cotton, and potatoes prior to harvest, and for reduction of sucker branch growth in hops.

The endothall formulation classes that are registered on food/feed crops include granular and soluble concentrate liquid (SC/L). Both formulation classes may be applied using waterborne, ground, or aerial equipment.

The most recent risk assessment was conducted in 2009 (D370448, D. Soderberg, 11/09/2009). An acute dietary point of departure (POD) was not selected since there was no appropriate endpoint attributable to a single dose in any of the studies submitted. The POD of 2 mg/kg/day was used to assess chronic dietary exposure was based on proliferative lesions of the gastric epithelium in both sexes at the lowest observed adverse effect level (LOAEL) in the 2-generation reproduction toxicity study in rats. An oral POD of 9.4 mg/kg/day was used to assess short-term incidental oral and inhalation risk based on decreased pup body weight (both sexes) seen on Day 0 in the F_1 and F_2 generations at the LOAEL of 60 mg/kg/day in the 2-generation rat reproduction (oral feeding) study. A dermal POD was not selected for endothall because the severe dermal irritation observed in a repeated-dose study was considered self-limiting. Current product labels recommend protective clothing (gloves, face shields, or goggles) when handling liquid formulations.

III. STUDY WAIVER REQUESTS

a. Neurotoxicity Screening Battery

Acute and subchronic neurotoxicity studies are required in the 2007 revised 40 CFR Part 158 Toxicology Data Requirements because they provide important scientific information on potential nervous system effects from pesticide exposure. These studies can provide data on a wide range of functional tests for evaluating neurotoxicity including sensory effects, neuromuscular effects, learning and memory and histopathology of the nervous system. The

HASPOC used a weight of the evidence (WOE) approach when considering the need for acute and subchronic neurotoxicity studies to support the registered and proposed uses of endothall.

- **Evidence for neurotoxicity in the endothall database of toxicology studies**: There are no clear signs of neurotoxicity following subchronic or chronic dosing in multiple species in the endothall database. In 2004, the HED Hazard Identification And Review Committee (HIARC) concluded that there was not a concern for neurotoxicity resulting from exposure to endothall. No clinical signs or symptoms of neurotoxicity/neuropathology were detected in any of the available guideline studies. The most common effect seen in the endothall toxicity database was decreased body weight.

- **Evidence for neurotoxicity in the database of toxicology studies for other carboxylic acid pesticides**: Endothall is a carboxylic acid pesticide. Other carboxylic acids include clopyralid, fluroxypyr, picloram, quinclorac, and aminopyralid. However, there is no evidence of neurotoxicity in the available toxicity studies for these chemicals. The HASPOC recently waived the required acute and subchronic neurotoxicity studies for quinclorac (TXR# 0056385) based on the lack of neurotoxic effects in the toxicity database, the low acute exposure risk estimates for quinclorac, that an acute neurotoxicity study would be unlikely to yield a lower POD for risk assessment, and the target organs of quinclorac were the liver and kidneys. Further, a search of the open literature and the HED's Integrated Structure, Toxicology, Endpoints and Properties (ISTEP) database did not provide data on neurotoxicity for these chemicals.

IV. HASPOC RECOMMENDATION

The HASPOC concludes, based on a WOE approach, that acute and subchronic neurotoxicity studies are not required for endothall at this time. This approach considered all of the available hazard and exposure information, including: (1) neurotoxic effects were not observed in the available acute, subchronic, chronic, developmental, and reproduction studies; (2) no neurotoxicity was observed in the databases of chemicals structurally similar to endothall; and (3) the most common effect seen in the endothall toxicity database was decreased body weight.